

Vaccination for herpes simplex genitalis

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SUMMARY Type-specific vaccines containing heat-inactivated herpes simplex hominis virus type 1 or 2 have been developed for the treatment of herpes simplex genitalis. When patients with recurrent herpes genitalis were treated with the type 2 vaccine the clinical course of the disease improved and the eruption-free interval was extended. In severe cases, especially in permanent genital herpes, the concurrent administration of vaccine and immunoglobulin concentrates improved the clinical course of the disease. Antibody titres and the *in-vitro* stimulation of lymphocytes with phytohaemagglutinin or herpes simplex hominis virus antigens remained constant during administration of the vaccine.

Introduction

Alterations in the cell-mediated immunity of patients with recurrent genital herpes have been observed by several authors using different methods. The studies (Lopez and O'Reilly, 1977; O'Reilly *et al.*, 1977; Wassilew and Koch, 1978) indicate a persistent or temporarily diminished immune response in patients with severe and frequently recurring genital herpes.

The mechanism that diminishes the immune response in these patients is unknown and we do not know if the diminished immune response to herpes simplex virus (HSV) antigens is the cause or an effect of the recurrence.

Findings in a rabbit model suggest that viral shedding can lead to a suppression or depletion of the function of T-lymphocytes (Cappel, 1976). If such is the case, efforts to augment the functional capacity of this population of lymphocytes might serve to increase the host's capacity to restrict viral proliferation and thereby reduce the frequency and the clinical manifestations of the infection.

Type-specific vaccines

Two type-specific vaccines have been developed in Germany; these contain heat-inactivated type 1 (Lupidon H®) or type 2 (Lupidon G®) herpes simplex hominis virus cultured aerobically on chick chorioallantoic membrane.

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The dosage and period of administration of the vaccine have to be adjusted to suit individual patients. A standard regimen for vaccination with the HSV type 2 antigen is a 1-ml dose containing 10^4 EID₅₀ (Wassilew and Koch, 1978); the dosage can be increased in severe cases up to 4 ml. The period of administration of the vaccine in many patients has to be extended to two to three years (Table).

SIDE EFFECTS

Up to now, no severe side effects of the vaccine therapy have been reported. In about 3% of patients local swelling has been observed. For theoretical reasons, the oncogenicity of the vaccine has been tested; no direct oncogenic effect with the HSV type 2 vaccine was found (Rapp, personal communication).

Results

Since 1971, the type 2 vaccine has been in clinical use and the results are encouraging. When patients have been treated for extended periods, there is clinical improvement in 60% to 100% of cases.

Table Vaccination regimen for herpes simplex genitalis with herpes simplex virus type 2 antigen (Lupidon G®)

Regimen (months)	Dosage	Frequency
First to third	1 ml	Each week
Fourth and fifth	1 ml	Every second week
Sixth to ninth	1 ml	Each month
For years	1 ml	Every second or third month

Raab summarised the results of different authors and found a mean improvement rate as high as 80% (Koinis and Wüthrich, 1975; Raab, 1977). A double-blind controlled study showed that the placebo without viral antigens brought no significant improvement (Weitgasser, 1977).

In 30 selected patients with immunoglobulin defects, mainly decreased IgG levels, Nasemann (1976) found that the concurrent administration of vaccine and immunoglobulin concentrates as adjuvants improved the clinical results. Of patients with herpes simplex type 2 infections which showed no improvement after vaccination alone, 62% reported improvement after treatment with vaccine and immunoglobulins combined. In double infections with both types of the virus, the improvement rate was lower. Especially in permanent (that is, fresh lesions arising before previous ones had healed) genital herpes, the combined therapy seemed to be indicated (Nasemann, 1976; Pra, 1977).

Clinical improvement is difficult to define in recurrent genital herpes. The natural course of the disease is unpredictable. We observed the patients weekly for three acute episodes before starting vaccination and for six months after completing vaccination. In our studies, we regarded a herpes-free interval after therapy which was twice as long as the interval before therapy as an improvement. Because clinical improvement is not objective, it seems essential to measure immunological parameters during vaccine therapy.

Remy *et al.* (1976) reported a follow-up study of antibody titres in patients treated with HSV type 2 vaccine. Over a period of nine months the titres remained almost constant; this suggests an important role for cell-mediated immunity in herpes recurrences.

Jarisch and Sandor (1977) examined the migration inhibitory factor production of lymphocytes in patients with recurrent herpes simplex during therapy, and indicated that migration inhibition paralleled the therapeutic effect in the treated patients.

We studied the specific and non-specific lymphocyte transformation before vaccination and four months later. A stimulation index (SI) was obtained by dividing impulses per minute (ipm) by tritiated thymidine-uptake in lymphocytes of cultures with antigen by the ipm of cultures without antigen. The phytohaemagglutinin (PHA) stimulation index and the SI by herpes simplex antigen (HSV) remained constant (Wassilew, 1979).

One patient had no further recurrences after vaccination. Six out of the 10 patients had only mild and short-term recurrences, and the herpes-free interval was at least twice as long after vaccination at four weeks. In four patients the course of the disease remained constant.

Conclusion

We believe that vaccination is of value in the treatment of recurrent herpes genitalis. For a better knowledge of the mode of action of the vaccine the patient should be kept under continuous observation.

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